Low Grade B Cell Lymphoma Arising in a Background of Multifocal Extra-Adrenal Myelolipoma

Aaron Noll¹, Jamie Boone¹, Mark Cunningham¹, Joshua Mammen², and Ossama Tawfik¹

¹Department of Pathology and Laboratory Medicine and ²Department of Surgery, University of Kansas Medical Center, Kansas City, KS, USA.

Abstract. Myelolipomas are rare, benign, non-functioning tumors composed of an admixture of mature adipose tissue and hematopoietic elements. Extra-adrenal myelolipomas are extremely rare, but have been reported in multiple sites including the omentum, presacral, and retroperitoneal areas, along with the thorax, kidneys, liver and stomach. We report a case of a 68-year-old man with low-grade B-cell lymphoma arising in a background of recurrent multifocal extra-adrenal myelolipoma. Pathological evaluation of the lesion and bone marrow showed foci of lymphoid aggregate that were confirmed to be monoclonal B lymphoma by flow cytometry. To our knowledge, this is only the third reported case to feature such a rare combination of diseases. The clinical, radiological, and pathological differential diagnostic findings are discussed.

Introduction

Myelolipoma is a rare benign tumor that consists of an admixture of mature adipose tissue and hematopoietic elements [1,2]. Classical myelolipomas are often incidentally discovered within the adrenal glands. Extra-adrenal myelolipoma is extremely rare, but has been reported in multiple sites including the omentum, presacral, and retroperitoneal areas, along with the thorax, kidneys, liver and stomach [2-6]. Similarly rare is the incidence of multifocal extra-adrenal myelolipomas and simultaneous cases of adrenal and extra-adrenal myelolipomas [2,7,8].

We report a rare case of low-grade B-cell lymphoma arising in a context of recurrent multifocal extra-adrenal myelolipoma in a 68-year-old patient. To our knowledge, this represents only the third reported case with such a unique combination of diseases. The clinical, radiological, and pathological differential diagnostic findings are discussed.

Case Report

Clinical Scenario. Approximately two years prior to his current admission in July 2012, a 68-year-old male was discovered to have a left-sided mass on abdominal examination by his primary care physician. The patient’s past medical history was significant for skin cancer on the forehead that was removed in 2005. Family history was significant for a mother who suffered from a rare combination of skin cancer and lymphoma and a father with bladder cancer. A subsequent CT scan revealed a large, complex left retroperitoneal mass with soft tissue components that displaced the left kidney and extended to the left iliac fossa. The vertical extent of the mass measured approximately 18.0 cm. Retroperitoneal lipomatous processes including lipoma and liposarcoma and other neoplastic processes were entertained radiologically in the differential diagnosis (Figure 1). A 501 gm 14.0 x 10.0 x 6.0 cm mass adherent to the retroperitoneum and below the left kidney was removed on exploratory laparotomy. Grossly, the lesion appeared predominately fatty with a yellow-red lobulated outer surface. Serial sectioning revealed a yellow-fatty, red hemorrhagic soft cut surface. Microscopic analysis showed classic features of myelolipoma with mature adipose tissue admixed with hematopoietic elements and evidence of extra-medullary hematopoiesis. Scattered lymphoid aggregates with monotonous, mature-appearing
lymphoid cells were noted throughout the lesion. CD3 and CD20 immunohistochemical stains showed the lymphoid aggregates to be composed of a mixed population of B and T cells. Cyclin D1 immunostains were negative. CD138 showed scattered plasma cells and in situ hybridization analysis confirmed the polyclonal expression of kappa and lambda light chains. The lymphomatous nature of these lymphoid aggregates was confirmed, however, by flow cytometry. Scattergram plots of the retroperitoneal mass flow results are shown in Figure 2. The lymphoid cells were gated, based on bright CD45 intensity and low side-scatter, and comprised 18% of the total cell population. The B cells were positive for CD19, CD20, and FMC7 with a monoclonal kappa light chain restriction and negative for CD5, CD10, CD23 and CD34. T cells showed a normal immunophenotype. The findings were conclusive for a low-grade B-cell lymphoma with an immunophenotype that was nonspecific for further subclassification.

On further evaluation of the patient, a bone marrow biopsy was performed showing a small focus of lymphoid aggregate (Figure 3) that was confirmed to be monoclonal B-cell lymphoma by flow cytometry. Lymphoid cells comprised 12% of all marrow cells. There was a predominance of T cells with a markedly increased CD4:CD8 ratio of 14.5:1. The B cells comprised 24% of the lymphoid cells and showed monotypic expression of kappa surface light chain (kappa:lambda ratio = 24:1). These immunophenotypic findings resembled those previously reported in the retroperitoneal mass. These monoclonal cells comprised 3% of all cells.

The patient was then started on standard chemotherapy to treat the lymphoma. A repeat abdominal CT with contrast was performed following surgical excision of the mass two weeks later. Studies showed persistence of the lipomatous retroperitoneal mass with numerous soft tissue nodules (Figure 4). The largest soft tissue component at the caudal margin of the lesion had decreased in size; however, the overall appearance was still more typical of a lipomatous tumor. That decrease in size was thought to represent either a rapid response to lymphoma therapy or possibly a decreasing post-surgical hematoma.

At the first six-month follow-up, because of the pathologic features of a low-grade lymphoma, a lack of B symptoms, and the major mass being composed of benign components, it was decided to wait and watch for disease progression instead of pursuing systemic chemotherapy.

At the second six-month follow-up, CT of the abdomen showed persistence of the ill-defined large left retroperitoneal lipomatous mass medial, posterior, and inferior to the left kidney. There were multiple soft tissue nodules within the lateral mass component. A PET-CT showed a very low level of metabolic activity associated with the irregular left retroperitoneal mass and fat stranding. At the third six-month follow-up, PET lymphoma impression demonstrated that the left retroperitoneal mass had increased in metabolic activity and was concerning for early lymphoma recurrence. At the fourth six-month follow-up, a CT with contrast demonstrated stability of the retroperitoneal mass, again with features consistent with a lipomatous process.

At the subsequent year’s follow-up, the patient returned to the clinic for routine surveillance. Colonoscopy showed seven tubular adenomas, which were removed. A large 3 cm mass in the cecum was also removed. In addition, a subsequent CT showed a new right retroperitoneal mass that was radiologically similar to the left peritoneal mass concerning for liposarcoma. The patient subsequently underwent an exploratory laparotomy, radical resection of left peritoneal mass, and right hemicolectomy.
Pathologic evaluation of the right colonic mass demonstrated a tubulovillous adenoma with no evidence of high-grade dysplasia or invasive carcinoma. Two large retroperitoneal masses, measuring 15 x 8.5 x 5.0 cm and 9.0 x 8.0 x 5.0 cm, were removed. Figures 5 and 6 highlight the gross and microscopic features of myelolipoma of these lesions. Similar to the originally resected mass, occasional lymphoid aggregates were noted (Figure 7).

Immunohistochemistry analyses of these aggregates were inconclusive for lymphoma, though flow cytometry confirmed the same monoclonal nature of these cells and the diagnosis of low-grade B-cell lymphoma. There was no evidence of liposarcoma, and cytogenetic analysis was reported to be normal. Extensive sampling of the tissue did not reveal any adrenal tissue in either specimen.

Figure 2. Flow cytometric analysis (scattergram plots) of the retroperitoneal mass at initial presentation, showing a subpopulation of monoclonal kappa B cells. A, CD45 versus side scatter plot showing bright CD45(+) lymphocytes in gate A (19.3% of total events). All subsequent scattergram plots (B to I) are based on gate A. B, CD19 versus kappa light chain plot showing CD19(+)-monoclonal kappa(+) B cells. C, CD19 versus lambda light chain plot. D, CD19 versus CD5 plot. E, CD19 versus CD10 plot. F, CD19 versus CD20 plot showing CD19(+), CD20(+) B cells. G, CD19 versus CD23 plot. H, CD19 versus CD34 plot. I, CD19 versus FMC7 plot showing CD19(+), FMC7(+) B cells.
Myelolipomas are rare, non-functioning benign tumors that were first described in 1905 by Gierke [1]. Myelolipomas are found to be more prevalent in females, with a male to female ratio of 1:2, and at the time of diagnosis, patients have a median age of 66.5 years [1,2]. The etiology of myelolipomas remains unclear [1]. The tumors are typically asymptomatic and are only identified incidentally upon imaging. Although the majority of myelolipomas are asymptomatic, in some cases they can cause vague abdominal symptoms including flank pain or nausea due to compression of surrounding structures, necrosis, or spontaneous retroperitoneal hemorrhage [2,9,10]. Surgical excision is usually only indicated if the mass becomes symptomatic; otherwise, it can be tracked by imaging studies [2]. Myelolipomas most commonly arise within the adrenal gland and comprise less than 4% of all adrenal tumors [2]. The occurrence of extra-adrenal myelolipomas is rare, with only approximately 50 cases reported within the last two decades [2,4]. Extra-adrenal myelolipomas range in size from 4 to 15 cm, with at least half occurring in the retroperitoneal pre-sacral soft tissue [1,3]. Other reported sites include the stomach, pelvis, thorax, and peri-renal soft tissue [2,4]. Bilateral/multifocal extra-adrenal myelolipomas have also been reported. To our knowledge, there have been only ten reported cases of bilateral/multifocal extra-adrenal myelolipomas [2,7,8,19-24].

Grossly, extra-adrenal myelolipomas are well-circumscribed masses that are yellow in color due to the predominance of adipose tissue [1,2]. Microscopically, the tumor is composed of adipose tissue with scattered hematopoietic elements [2]. Imaging features of myelolipomas depend on the major component of the mass [11]. Characteristics such as location, size, vascularity, and local invasion can help establish an extra-adrenal myelolipoma diagnosis [11]. Adrenal myelolipomas are easily identified by either CT or MR imaging as lipid-like adrenal masses [12,13]. Although outside of the adrenal gland, they may appear virtually identical to other soft-tissue tumors [12-15]. Distinguishing extra-adrenal myelolipomas from lipomas, retroperitoneal myolipomas, extra-medullary hematopoietic tumors, angiomyolipoma, and

**Figure 3.** Bone marrow biopsy showing a small focus of lymphoid aggregate that was confirmed to be monoclonal B cell lymphoma by flow cytometry (Hematoxylin and eosin, 200x).

**Figure 4.** Coronal CT abdomen with contrast. Status post surgical excision of a 501 gm 14.0 x 10.0 x 6.0 cm mass. Persistent mass on left with numerous soft tissue nodules.

**Figure 5.** Gross photo of the left retroperitoneal myelolipoma.
well-differentiated liposarcomas on imaging may prove to be a formidable task [11,12,14,15]. Extra-adrenal myelolipomas are normally well encapsulated, whereas liposarcomas tend to be poorly marginated [12]. Myolipomas are made of variable amounts of mature adipose tissue and smooth muscle cells. If hemorrhage is a feature of a myolipoma, then it is doubtful that one could differentiate it from an extra-adrenal myelolipoma using imaging alone [12]. Angiomyolipomas have prominent vascular structures in addition to the classic myelolipoma features [11]. Myelolipoma and extra-medullary hematopoiesis may have similar appearances on imaging [10]. Therefore biopsy is often necessary to confirm the diagnosis of extra-adrenal myelolipoma [11,15].

The finding of lymphoid aggregates in our reported case was not a unique finding for myelolipomas. Increased lymphoid aggregates have been previously described in myelolipomas. In a study done by Saboorian and colleagues, flow cytometric analysis was run on the tissue of myelolipomas with increased lymphoid aggregates, unremarkable T cells, polyclonal B cells, and a small portion of NK cells with no phenotypic aberrations or B-cell hematopoiesis. The distinction can be very difficult to make clinically, radiographically, and histologically [2]. Features suggesting extra-medullary hematopoiesis include a younger age of onset (median 43.7 years), multifocality, association with unexplained splenomegaly (80%) and/or hepatomegaly (58%), and the histological demonstration of erythroid hyperplasia with absence of lymphoid aggregates [1,2].
monoclonality [1,16]. However, the finding of a monoclonal population of B cells within the lymphoid aggregates on flow cytometry and the subsequent diagnosis of low-grade B-cell lymphoma arising in a myelolipoma of our case was a unique finding. To our knowledge, only three other cases of lymphoma arising in a myelolipoma have been previously reported, and none were demonstrated by flow cytometry. Of the three reported cases, the first was a case of Hodgkin’s lymphoma, the second of small lymphocytic lymphoma/chronic lymphocytic leukemia, and the third of chronic lymphocytic leukemia [1,17,18].

In conclusion, the reported case showed findings of a low-grade B-cell lymphoma arising in a background of an extra-adrenal myelolipoma. Imaging studies differentiating this rare extra-adrenal myelolipomas from other soft tissue tumors could be challenging. A superimposed collision neoplastic process is even more challenging. A high index of clinical suspicion and careful pathologic evaluation is recommended for the accurate diagnosis of such lesions. The flow cytometry findings of a monoclonal B-cell population truly made this case unique.

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References